Hypertension

Outpatient Hypertension Control and Prescribing Habits for Hypertension in Taiwan

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Background: Hypertension control is of the utmost importance for reducing cardiovascular risk. In Taiwan, the hypertension control rate of the general population is low (25%). We investigated the factors affecting outpatient hypertension control to determine whether the low control rate stems from clinician unawareness or inadequate public education.

Methods: Hypertensive patients were recruited between 2003 and 2004 by 13 cardiologists and 9 non-cardiologists from 19 hospitals distributed across four geographical areas of Taiwan. Each clinician recruited 100 consecutive patients from outpatient clinics and reported their drug prescriptions, co-morbidities, and blood pressure (BP) levels. Data were analyzed using the chi square test and multivariate logistic regression analyses.

Results: Of the 2145 enrolled patients, 63% attained the BP goal of < 140/90 mmHg. BP control rates were higher in older patients, and in patients who were treated by cardiologists and at medical centers. The control rate of high risk co-morbidity patients (BP goal of < 130/80 mmHg) was 36%, which was significantly lower than the 62% control rate of low risk patients (BP goal of < 140/90 mmHg). Cardiologists achieved higher BP control rates (65% vs. 60%; p = 0.0039), and prescribed more combination regimens (p < 0.0001) and beta blockers than non-cardiologists. Overall, 63% of patients received combination therapy. Calcium channel blockers were the most commonly prescribed antihypertensive drugs, followed by beta blockers, angiotensin receptor blockers, diuretics, and angiotensin-converting enzyme inhibitors.

Conclusions: Two-thirds of the entire study population received combination therapy, although BP control rate is still less than optimal in the high risk patients. Ultimately, a more aggressive strategy is strongly encouraged for patients considered to be at high risk.

Key Words: Combination therapy • Hypertension control rate • Prescribing habit

INTRODUCTION

It is well-documented that blood pressure (BP) control leads to a reduction in cardiovascular disease risk.[1] Since the implementation of Taiwan's National Health Insurance (NHI) program in 1995, medical services have become more accessible to the general population. Ninety-six percent of Taiwanese citizens are covered by this program, and by 1996, ninety percent of hospitals and clinics were NHI-funded healthcare providers.[2,3] Consequently, favorable changes in education and the availability of care may have accounted for improvements seen in the control of hypertension in Taiwan. That is, in 2002, significant improvements in hyperten-

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sion awareness (i.e., 56% of males, 74% of females), treatment (i.e., 44% of males, 59% of females), and control (i.e., 21% of males, 29% of females) were reported for hypertensive patients aged 19 years and older.[4] Despite this, the hypertension control rates in Taiwan are still lower than those reported in the United States, particularly for males (i.e., 33% in males, 30% in females).[5] It is unknown whether the lower hypertension control rates either reflect physician unawareness of BP targets or may be due to inadequate public education in Taiwan. Thus, to answer this question, we investigated the factors affecting outpatient hypertension control and prescribing habits for hypertension of different subspecialists at various clinics in Taiwan.

METHODS

Participating hospitals and physicians

The data used for the present study were retrieved from a nested cross-sectional study that studied the effects of hypertensive treatment on serum uric acid concentration levels and renal function in Taiwan. We accessed the same database, as the timing of our study (2003-2004) was subsequent to that of the Taiwanese Survey on Hypertension, Hyperglycemia, and Hyperlipidemia (TwSHHH), which was conducted in 2002.[4] Additionally, our database was also available for assessing outpatient BP control in Taiwanese hospitals during that period. For the study, we divided Taiwan into four areas, namely the North, Central, South, and East Coast, according to geographical characteristics and urbanization indices. The population of Taiwan is approximately 23 million, with the North area being the most modernized and the East Coast area being the least modernized.

Various hospitals located in either metropolitan or provincial cities were selected for the study according to population density. These included nine hospitals in the North (i.e., 2 medical centers, 5 regional hospitals, and 2 district hospitals), four hospitals in the Central region (i.e., 1 medical center, 2 regional hospitals, and 1 district hospital), four hospitals in the South (i.e., 3 regional hospitals and 1 district hospital), and two hospitals in the East Coast area (i.e., 1 regional hospital and 1 district hospital). Twenty-two physicians participated in this study, specifically 13 cardiologists, four diabetologists, two family medicine physicians, one nephrologist, one neurologist, and one gastroenterologist.

Patient population

The protocol and consent forms for this study were approved by the Chung Shan Medical University Hospital Institutional Review Board. Each physician at a participating hospital outpatient clinic identified and consecutively recruited 100 patients diagnosed with essential hypertension between September 2003 and December 2004. Each study participant was briefed on the purpose, procedure, and potential risks and benefits of the study. All participants also provided written informed consent before any study procedure was conducted.

During the recruitment period, patients 20 years of age or older who for the first time visited the outpatient clinics of the participating hospitals for routine check-up or evaluation/follow-up for their hypertension were enrolled in the study. Eligible male or female patients were required to have a diagnosis of essential hypertension without any other concomitant medical problem, and have the ability to understand and answer the symptom assessment questionnaire used in the study. BP was measured on the patient's right upper arm in the sitting position. At least two measurements were taken with a 5-minute interval, and the second blood pressure reading was used in the data analysis. To be eligible, male or female patients required a diagnosis of essential hypertension, which was defined as a systolic blood pressure (SBP) $\geq$ 140 mmHg and/or diastolic blood pressure (DBP) $\geq$ 90 mmHg, and had to be undergoing treatment with antihypertensive medications. Patients were excluded if they had a diagnosis of secondary hypertension, a history of malignant hypertension or a history of cerebrovascular accident or transient ischemic attack within 6 months prior to enrollment, a sitting systolic blood pressure greater than 210 mmHg at baseline, a confirmed myocardial infarction or episode of angina pectoris, or a clinically significant cardiac arrhythmia within the 12 months prior to enrollment. Patients were also excluded if they had hemodynamically significant valvular disease or cardiomyopathy, had undergone percutaneous coronary angioplasty or coronary artery bypass surgery within the prior 6 months, or had uncontrolled diabetes mellitus, renal

disease, neurological disorder, cardiovascular, hepatic or neoplastic disease.

Data collection and assessment of variables

Demographic information, antihypertensive treatment regimens, duration of hypertension, SBP and DBP values, body mass index, and co-morbidities (e.g., cardiovascular disease, cerebral vascular disease, kidney disease, and diabetes) were recorded. The overall goal of treatment was to reduce BP to a value of < 140/90 mmHg in the general population, and < 130/80 mmHg in high risk patients with either kidney disease, diabetes, or associated cardiovascular or cerebrovascular disease.

Statistical analysis

Statistical analysis was performed by using the SAS statistical package (version 8.2e, SAS Institute, Cary, North Carolina, USA). The Chi-square test was carried out to determine the statistical significance of the differences between variables. Multivariate logistic regression analyses were performed to identify the independent factors associated with BP control rates, prescription patterns of monotherapy and combination therapy with antihypertensive drugs, and prescription rates of the different antihypertensive drug classes. All tests were two-sided, and values of $p < 0.05$ were considered statistically significant. Whenever multiple comparisons were performed, Bonferroni adjustments were made accordingly. Odds ratios (OR) are presented with 95% confidence intervals (95% CI).

RESULTS

A total of 2187 patients were recruited, 42 of whom were excluded due to insufficient data. Thus, data were analyzed for a total of 2145 patients (1139 males with a mean age of 64 $\pm$ 13 years; 1006 females with a mean age of 64 $\pm$ 11 years). All individuals were being treated with antihypertensive medications, and approximately half had been diagnosed with hypertension for at least five years. The BP goal (< 140/90 mmHg) achievement rate was significantly higher in patients treated at medical centers (OR 2.85, 95% CI 1.94 to 4.18) and patients treated by cardiologists (OR 1.49, 95% CI 1.14 to 1.95) (Table 1). Younger patients had a significantly lower BP goal achievement rate (OR 0.70, 95% CI 0.51 to 0.96). Overall, the BP control rate was 63% for all patients. However, the BP control rate for high risk patients with co-morbidities was only 36% (i.e., 35% in patients with diabetes; 31% in patients with kidney disease; 31% in patients with cardiac disease; 36% in patients with cerebral vascular disease), which was significantly lower (OR 0.35, 95% CI 0.24 to 0.53) than that of patients without co-morbidities (62%). Findings with respect to prescription patterns are presented in Table 2. Cardiologists were more likely to prescribe combination therapy than non-cardiologists. District hospitals were more likely to prescribe monotherapy than other institutions. Patients with longer durations of hypertension and those with co-morbidities were more likely to receive combination therapy consisting of $\geq$ 3 antihypertensive agents. Males were more likely to receive $\geq$ 3 antihypertensive agents than females. Furthermore, the prescribing habits of cardiologists and non-cardiologists were assessed according to hypertension duration (Figure 1). Cardiologists achieved a higher BP control rate ($p < 0.01$) with monotherapy, and prescribed combination regimens more aggressively in patients with prolonged hypertension than non-cardiologists ($p < 0.0001$). There were no significant differences between cardiologists and non-cardiologists in achieving BP control (< 130/80 mmHg) in high risk patients with diabetes (36% vs. 35%), kidney disease (33% vs. 30%), cardiovascular disease (39% vs. 33%), or cerebrovascular disease (36% vs. 35%).

Table 3 presents the prescribing habits for hypertension according to antihypertensive drug class. Angiotensin converting enzyme (ACE) inhibitors were prescribed more frequently in males (OR 1.57, 95% CI 1.26 to 1.97), diabetes patients (OR 1.40, 95% CI 1.09 to 1.79) and patients with cerebrovascular disease (OR 1.70, 95% CI 1.20 to 2.42). Furthermore, district hospitals prescribed ACE inhibitors less frequently (OR 0.66, 95% CI 0.45 to 0.99) than other institutions. β blockers (BBs) were prescribed more frequently by cardiologists (OR 3.15; 95% CI 2.50 to 3.96) and hospitals in the North, whereas BBs were prescribed less frequently to males (OR 0.81, 95% CI 0.67 to 0.98) and at district hospitals (OR 0.72, 95% CI 0.53 to 0.99). Older patients (OR 1.56, 95% CI 1.06 to 2.29), and patients with cardiovascular disease (OR 1.58, 95% CI 1.24 to 2.02) and kidney disease (OR 1.89, 95% CI 1.23 to 2.90) were pre-

Table 1. Blood pressure goal achievement among hypertensive patients in Taiwan

		N	Control (%)	Adjusted OR	95% CI	p value
Sex	Male	1139	522 (45.83)	0.96	0.79, 1.18	0.71
	Female (R)	1006	479 (47.61)	1.00		
Age (years)	20-49	243	103 (42.39)	0.70	0.51, 0.96	0.026*
	≥ 50 (R)	1854	875 (47.20)	1.00		
BMI (kg/m^2)	≥ 27	707	306 (43.28)	0.90	0.73, 1.11	0.33
	< 27 (R)	1270	601 (47.32)	1.00		
Duration of hypertension	≥ 5	1031	468 (45.39)	0.85	0.69, 1.05	0.13
(years)	< 5 (R)	1000	482 (48.20)	1.00		
Hospital location	North	1188	568 (47.81)	0.82	0.56, 1.19	0.30
	Center	423	201 (47.52)	0.68	0.45, 1.01	0.05
	South	342	145 (42.40)	0.93	0.62, 1.39	0.71
	East (R)	192	87 (45.31)	1.00		
Hospital facility	Medical center	471	277 (58.81)	2.85	1.94, 4.18	< 0.001*
	Regional hospital	1267	525 (41.44)	0.84	0.61, 1.17	0.31
	District hospital (R)	407	199 (48.89)	1.00		
Physician's sub-specialist	Cardiologist	1198	614 (51.25)	1.49	1.14, 1.95	0.004*
	Non-cardiologist (R)	947	387 (40.87)	1.00		
Prescription pattern	Monotherapy (R)	775	367 (47.35)	1.00		
	Two-drug combination	864	411 (47.57)	0.91	0.73, 1.15	0.43
	Three-drug combination	388	170 (43.81)	0.84	0.63, 1.13	0.25
	Four-drug (+) combination	75	37 (49.33)	1.20	0.70, 2.08	0.51
Patients with co-morbidity	Diabetes (goal < 130/80 mmHg)	819	289 (35.29)	0.89	0.63, 1.26	0.50
vs. without co-morbidity	Kidney disease (goal < 130/80 mmHg)	124	38 (30.65)	0.89	0.56, 1.41	0.62
	Cardiac disease (goal < 130/80 mmHg)	571	213 (37.30)	1.09	0.78, 1.52	0.62
	Cerebrovascular disease (goal < 130/80 mmHg)	195	70 (35.90)	1.02	0.70, 1.48	0.92
	All co-morbidity patients (goal < 130/80 mmHg)	1272	460 (36.16)	0.35	0.24, 0.53	< 0.001*
	Patients with no co-morbidity (goal < 140/90 mmHg)	873	541 (61.97)	1.00		

BMI, body mass index; CI, confidence interval; Control, number of hypertensive controls; N, number; OR, odds ratio; R, reference.
* Indicates statistically significant difference, odds ratio were fully adjusted for all variables.

scribed diuretics more often, whereas diuretics were prescribed less often at district hospitals (OR 0.612, 95% CI 0.40 to 0.94). Angiotensin receptor blockers (ARBs) were more commonly prescribed to patients with cardiovascular disease (OR 1.43, 95% CI 1.16 to 1.77) and diabetes (OR 1.25, 95% CI 1.01 to 1.53), as well as those attending hospitals in the South region (OR 1.416, 95% CI 1.084 to 1.850).

Figure 2 presents the prescription patterns according to antihypertensive drug class. CCBs (31%) were the most prescribed antihypertensive drug, followed by BBs (21%), ARBs (21%), ACE inhibitors (11%), and diuretics (11%), whereas α blockers were the least prescribed (5%). Additionally, CCBs were the most common antihypertensives used in combination therapy. Sixty-three percent of patients received more than two antihypertensive drugs from different drug classes. The proportions of patients who received combinations of two, three, and four or more drug therapies were 41%, 18%, and 4%, respectively.

DISCUSSION

The findings of the present study indicate that there was a high success rate of 63% in achieving the BP goal of < 140/90 mmHg in outpatient clinics of hospitals in Taiwan. Additionally, combination therapy with multiple

Table 2. Effects of patient gender and age, physician specialty, hospital type and location, patient's co-morbidities, and duration of hypertension on prescription patterns according to antihypertensive therapy regimen

Variables	Monotherapy				2-Combination therapy				≥ 3-combination therapy				Total prescription N
	N (%)	Adjusted OR	95% CI	p value	N (%)	Adjusted OR	95% CI	p value	N (%)	Adjusted OR	95% CI	p value	
Patient gender													
Male	386 (34.62%)	0.87	0.72, 1.05	0.15	445 (39.91%)	0.88	0.74, 1.06	0.18	284 (25.47%)	1.41	1.13, 1.78	0.003*	1115
Female (R)	389 (39.41%)	1.00			419 (42.45%)	1.00			179 (18.14%)	1.00			987
Patient age (years)													
< 50	98 (41.35%)	1.18	0.88, 1.58	0.27	95 (40.08%)	0.92	0.69, 1.23	0.57	44 (18.57%)	0.90	0.62, 1.31	0.59	237
≥ 50 (R)	655 (36.05%)	1.00			755 (41.55%)	1.00			407 (22.40%)	1.00			1817
Physician specialist													
Cardiologists	359 (30.40%)	0.45	0.36, 0.56	< 0.001*	507 (42.93%)	1.26	1.01, 1.56	0.039*	315 (26.67%)	2.56	1.95, 3.37	< 0.001*	1181
Non-cardiologists (R)	416 (45.17%)	1.00			357 (38.76%)	1.00			148 (16.07%)	1.00			921
Class of hospital facility													
Medical centers	163 (35.21%)	0.49	0.36, 0.67	< 0.001*	206 (44.49%)	1.84	1.35, 2.50	0.001*	94 (20.30%)	1.43	0.96, 2.14	0.08	463
Regional hospitals	412 (32.93%)	0.60	0.47, 0.77	< 0.001*	524 (41.89%)	1.45	1.13, 1.87	0.004*	315 (25.18%)	1.58	1.14, 2.20	0.006*	1251
District hospitals (R)	200 (51.55%)	1.00			134 (34.54%)	1.00			54 (13.92%)	1.00			388
Hospital location													
North	424 (36.09%)	1.26	0.87, 1.81	0.22	468 (39.83%)	0.79	0.57, 1.11	0.18	283 (24.09%)	1.25	0.82, 1.92	0.30	1175
Center	135 (32.77%)	1.27	0.84, 1.92	0.25	187 (45.39%)	0.96	0.66, 1.40	0.84	90 (21.84%)	0.83	0.52, 1.32	0.43	412
South	142 (43.29%)	1.26	0.85, 1.87	0.25	133 (40.55%)	0.89	0.61, 1.29	0.54	53 (16.16%)	0.81	0.49, 1.33	0.41	328
East (R)	74 (39.57%)	1.00			76 (40.64%)	1.00			37 (19.79%)	1.00			187
Duration of hypertension													
< 5 ears (R)	426 (43.83%)	1.00			383 (39.40%)	1.00			163 (16.77%)	1.00			972
≥ 5 years	317 (31.17%)	0.61	0.50, 0.75	< 0.001*	438 (43.07%)	1.19	0.99, 1.44	0.07	262 (25.76%)	1.63	1.29, 2.06	< 0.001*	1017
Co-morbidity													
With	445 (35.60%)	0.79	0.65, 0.97	0.022*	509 (40.72%)	1.03	0.85, 1.24	0.79	296 (23.68%)	1.37	1.08, 1.74	0.009*	1250
Without (R)	330 (38.73%)	1.00			355 (41.67%)	1.00			167 (19.60%)	1.00			852
Total N	775				864				463				2102

As listed in Table 1; R, reference. Odds ratios (OR) were fully adjusted for all variables.

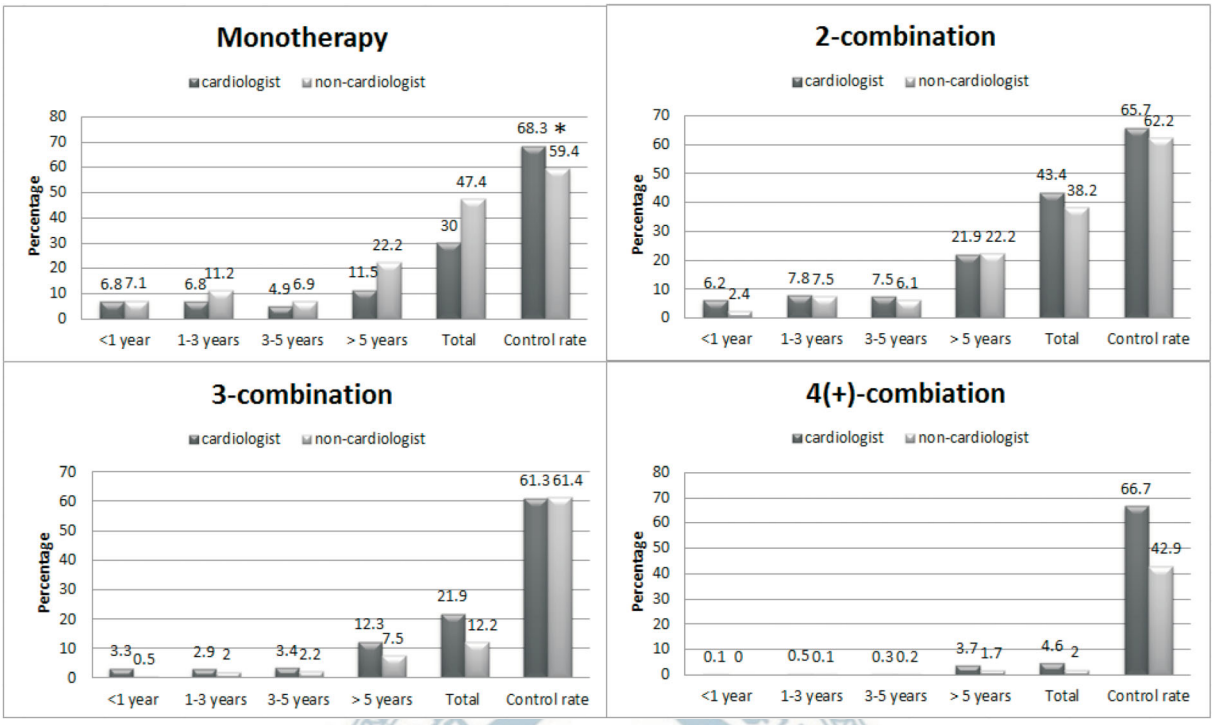

Figure 1. *The prescribing habits of cardiologists and non-cardiologists at outpatient clinics according to hypertension duration. Cardiologists prescribed combination regimens more aggressively in patients with prolonged hypertension than non-cardiologists ($p < 0.0001$) and achieved a significantly higher BP control rate in monotherapy group ($p < 0.01$, indicated by *).*

antihypertensive drugs was prescribed in 63% of patients. Cardiologists had a significantly greater success rate in achieving BP goals and were more aggressive to prescribe combination regimens and BBs than non-cardiologists. In high risk patients with co-morbidities, such as diabetes, kidney diseases, cardiac diseases, and cerebrovascular diseases, the BP goal of < 130/80 mmHg was achieved in only 36% of patients. CCBs were the most commonly prescribed antihypertensive drugs, whereas diuretics and ACE inhibitors were the least prescribed. This is the first survey to demonstrate a high discrepancy in BP control among hypertensive patients visiting outpatient clinics (63%) and the general population (25%) in Taiwan. The relatively low BP control rate in the general population compared to hypertensive patients visiting outpatient clinics in Taiwan is likely due to a lack of public education. These findings may influence the nationwide healthcare policies and population education with respect to cardiovascular disease in Taiwan. Additionally, these findings can serve as a reference for healthcare policymakers in their attempts to facilitate hypertension control.

It has been well documented that BP control leads to a reduction in cardiovascular disease risk.[6] A meta-analysis of 61 cohort studies involving 1,000,000 participants demonstrated that small differences in BP can account for large differences in cardiovascular disease outcomes.[7] Epidemiological assessments of the prevalence of hypertension and awareness, treatment, and control of BP in the general population are important for evaluating the effects of healthcare policy implementation. Su et al. reported that, after the implementation of the NHI program in 1995, there were significant improvements in hypertension awareness (i.e., 56% of males, 74% of females), treatment (i.e., 44% of males, 59% of females), and control (i.e., 21% of males, 29% of females) among hypertensive patients aged 19 years and older in Taiwan in 2002 compared to 1993-1996 (awareness: 23% of males and 39% of females; treatment: 13% of males and 28% of females; and control: 2% of males and 5% of females).[4] This BP control rate is, however, still lower than that reported in the United States, particularly for males (i.e., 33% of males and 30% of females).[5]

Table 3. Effects of patient demographics, physician specialty, geographical region, co-morbidities, and type of hospital facility on the likelihood of receiving a certain antihypertensive drug class for the treatment of hypertension in outpatient clinics

Variables	Diuretics		BB		CCB		ACE inhibitors		ARB	
	No. (%)	Adjusted OR (95% CI)	No. (%)	Adjusted OR (95% CI)	No. (%)	Adjusted OR (95% CI)	No. (%)	Adjusted OR (95% CI)	No. (%)	Adjusted OR (95% CI)
Gender										
Female (R)	214 (21.3)	1.00	390 (38.8)	1.00	585 (58.2)	1.00	160 (15.9)	1.00	403 (40.1)	1.00
Male	223 (19.6)	NS	424 (37.2)	0.81* (0.67, 0.98)	662 (58.1)	NS	268 (23.5)	1.57* (1.26, 1.97)	438 (38.5)	NS
Age (years)										
20-49 (R)	35 (14.4)	1.00	101 (41.6)	1.00	137 (56.4)	1.00	55 (22.6)	1.00	85 (35.0)	1.00
≥ 50	393 (21.2)	1.56* (1.06, 2.29)	690 (37.2)	NS	1082 (58.4)	NS	364 (19.6)	NS	739 (39.9)	NS
Cardiologist	259 (21.6)	NS	563 (47.0)	3.15* (2.50, 3.96)	696 (58.1)	NS	245 (20.5)	NS	477 (39.8)	NS
Non-cardiologist (R)	178 (18.8)	1.00	251 (26.5)	1.00	551 (58.2)	1.00	183 (19.3)	1.00	364 (38.4)	1.00
Region										
North (R)	258 (21.7)	1.00	503 (42.3)	1.00	694 (58.4)	1.00	255 (21.5)	1.00	447 (37.6)	1.00
Center	81 (19.2)	NS	159 (37.6)	0.44* (0.34, 0.57)	255 (60.3)	NS	80 (18.9)	NS	167 (39.5)	NS
South	65 (19.0)	NS	93 (27.2)	0.50* (0.37, 0.67)	174 (50.9)	0.76* (0.59, 0.99)	64 (18.7)	NS	145 (42.4)	1.42* (1.08, 1.85)
East	33 (17.2)	NS	59 (30.7)	0.56* (0.39, 0.81)	124 (64.6)	1.47* (1.04, 2.07)	29 (15.1)	NS	82 (42.7)	NS
No co-morbidity	163 (18.7)	1.00	367 (42.0)	1.00	506 (58.0)	1.00	145 (16.6)	1.00	305 (34.9)	1.00
Co-morbidity	274 (21.5)		447 (35.1)		741 (58.3)		283 (22.3)		536 (42.1)	
Diabetes mellitus	143 (17.5)	0.75* (0.58, 0.96)	266 (32.5)	NS	478 (58.4)	NS	183 (22.3)	1.40* (1.09, 1.79)	350 (42.7)	1.25* (1.01, 1.53)
Cardiovascular disease	158 (27.7)	1.58* (1.24, 2.02)	249 (43.6)	NS	330 (57.8)	NS	127 (22.2)	NS	254 (44.5)	1.43* (1.16, 1.77)
Cerebrovascular disease	32 (16.4)	NS	75 (38.5)	NS	127 (65.1)	NS	55 (28.2)	1.70* (1.20, 2.42)	72 (36.9)	NS
Kidney disease	37 (29.8)	1.89* (1.23, 2.90)	45 (36.2)	NS	65 (52.4)	NS	31 (25.0)	NS	49 (39.5)	NS
Hospital facility										
Medical center (R)	79 (16.8)	1.000	185 (39.3)	1.00	275 (58.4)	1.00	99 (21.0)	1.00	203 (43.1)	1.00
Regional hospital	313 (24.7)	1.40* (1.03, 1.90)	502 (39.6)	NS	766 (60.5)	NS	276 (21.8)	NS	470 (37.1)	0.68* (0.54, 0.87)
District hospital	45 (11.1)	0.61* (0.40, 0.94)	127 (31.2)	0.72* (0.53, 0.99)	206 (50.6)	0.73* (0.54, 0.98)	53 (13.0)	0.66* (0.45, 0.99)	168 (41.3)	NS
Total No. (%)	437 (20.8)		814 (38.7)		1247 (59.3)		428 (20.4)		841 (38.7)	

The odds ratio (OR) was fully adjusted for all other variables listed in the table. * Indicates statistically significant differences.

ACE, angiotensin converting enzyme inhibitors; ARB, angiotensin receptor blockers; BB, beta blockers; CCB, calcium channel blockers; NS, statistically no significant differences; R, reference.

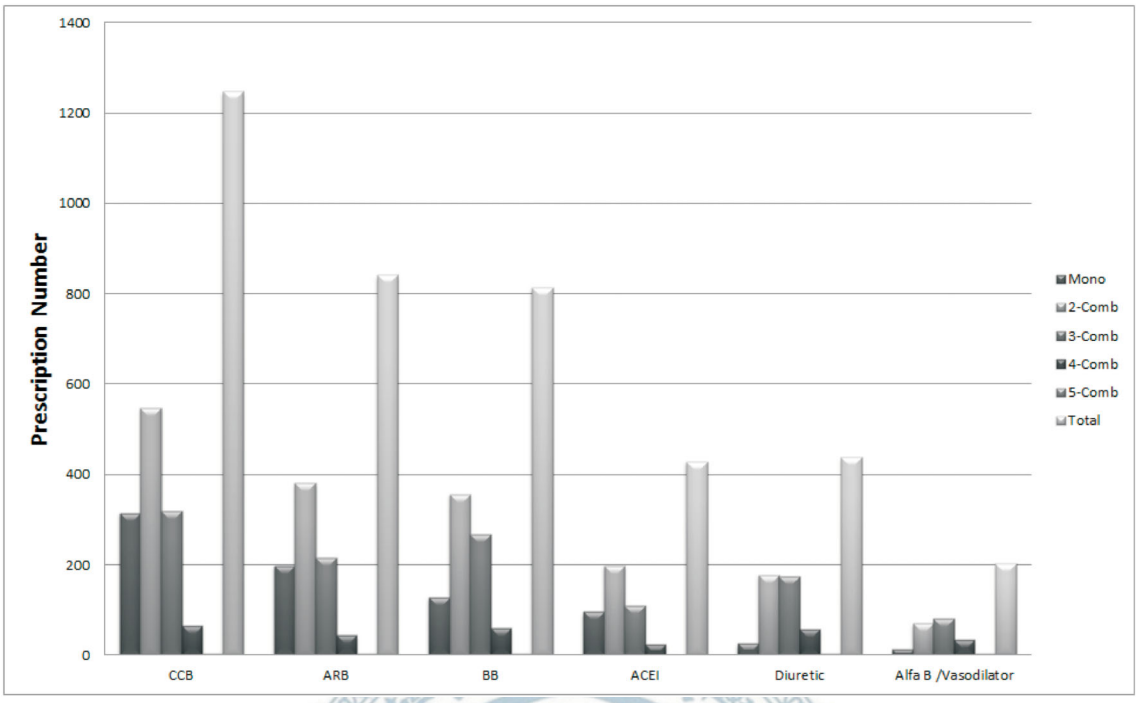

Figure 2. *Prescription patterns according to antihypertensive drug class. Calcium channel blockers (CCB) (31%) were the most commonly prescribed antihypertensive drugs, followed by β blockers (BB) (21%), angiotensin receptor blockers (ARB) (21%), angiotensin converting enzyme inhibitors (ACEI) (11%), and diuretics (11%), whereas α blockers (Alpha B) and vasodilators (5%) were the least prescribed. Abbreviations: Mono, monotherapy; 2-Comb, combination of two drug classes; 3-Comb, combination of three drug classes; 4-Comb, combination of four drug classes; 5-Comb, combination of five drug classes.*

The BP control rate is highly correlated with the awareness of the general population, as well as the physician's treatment behavior. Previous studies have shown that combination therapy with multiple antihypertensive drugs may improve BP control and reduce the incidence of side effects.[8] Law et al. performed a meta-analysis of 354 randomized double-blind controlled hypertension trials and showed a benefit of low-dose drug combinations, which increased efficacy and reduced adverse effects.[9] According to observations from the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT),[10] about 75% of patients with hypertension require therapy with more than one antihypertensive agent to achieve recommended BP goals. Corraro et al. found that patients starting on combination therapy had an additional 11% cardiovascular risk reduction compared to those starting on monotherapy.[11] Thus, prescribing combination therapy is important for patients with inadequate BP control. Our study findings suggest that 63% of patients in Taiwan are receiving combination therapy and that the same proportion of patients achieve BP targets. Thus, in Taiwan, physicians appear to making an effort in achieving BP goals. It was also found that cardiologists, medical centers, co-morbidity patients prescribing more combination therapy and cardiologists are more aggressive in prescribed more combination regimens to longer duration hypertensive patients (Figure 1) and achieved a greater BP control rates in the monotherapy group than non-cardiologists (68.3% vs. 59.4%, $p < 0.01$). These prescribing habits may be, in part, important factors in successful BP control. Furthermore, it was found that the drug classes prescribed to high-risk patients generally followed the guideline recommendations, such as the use of ACE inhibitors or ARBs in diabetes patients, ARBs among patients with cardiovascular disease, ACE inhibitors and CCBs in individuals with cerebrovascular disease.[12,13]

Hajjar et al. reported on the prevalence, awareness, treatment, and control of hypertension in the United States between 1988 and 2000.[5] They found that the BP control rate was 33% among males and 30% among

females. Conversely, in 2004, Wang et al. reported that the BP goal achievement rate of primary care physicians at outpatient clinics in the United States was 63% and in Europe was 31-46%.[14] Obviously, the BP control rate of outpatient clinics in the United States (63%) is considerably higher than that of the general population (31%). In the present study, an even greater discrepancy was observed, as the BP control rate of outpatient clinics in Taiwan was 63% compared to 25% in the general population. This observation suggests that public education and awareness regarding the BP goals for hypertensive patients is insufficient in Taiwan. White reviewed antihypertensive drug treatment strategies and concluded that the most important goal of therapy should be the use of combinations of additive or synergistic agents that improve efficacy in BP control.[15] Physician and general public awareness of the degree to which antihypertensive drugs are effective in reducing BP is essential for reducing the risk of cardiovascular events.

Management of high risk patients with hypertension has become more challenging in recent years. A BP < 130/80 mmHg is recommended by most hypertension treatment guidelines for patients in high risk groups.[12,13] In Taiwan, there are diminished rates of success in attaining BP levels below 130/80 mmHg among patients with diabetes (35%), cardiovascular diseases (37%), kidney disease (31%), and cerebrovascular disease (36%). In the present study, the BP control rate of diabetes patients corroborates with the rate reported by the National Diabetes Health Promotion Centers in Taiwan in 2006.[16] This lack of BP control is of particular concern. Nevertheless, it should be mentioned that high risk patients tend to be elderly and those with higher pretreatment BP levels, and thus, are inherently more difficult to control. Accordingly, most high risk patients with unacceptably high rates of prior BP control will require combination therapies, as recommended by the hypertension guidelines.[12,13]

In the present study, CCBs were the most commonly prescribed class of antihypertensive drugs, either as monotherapy or in combination (31%). BBs and ARBs were the second most prescribed (21%), and diuretics (11%) and ACE inhibitors (11%) were the least prescribed. These observations are in accordance with Liu et al., who studied prescription patterns in Taiwan using data from the computerized reimbursement database of the National Health Insurance between 1997 and 2004.[17] However, these prescription patterns are substantially different from those reported in 2004 in the United States, where diuretics were the most commonly prescribed antihypertensive agents (53%) and ARBs were the least prescribed (23%).[18] Diuretic use in Taiwan is also less common than in European countries (29 to 31%).[19] The two most commonly used two-drug combinations in Taiwan were CCBs plus ARBs (32%) and CCBs plus BBs (32%), and CCBs were the most commonly used drugs in combination therapy. On average, only 31% of combination therapy regimens included a diuretic, a much lower rate than that of the United States (71%).[18] Many clinicians in Taiwan seem to be concerned about the adverse side effect of diuretics, such as fatigue, and metabolite and electrolyte disturbances, and are hesitant to prescribe diuretics to their hypertensive patients. Additionally, a previous study in Taiwan noted a high prevalence of hyperuricemia (i.e., 22% in males and 24% in females) in the general population and in hypertensive patients (i.e., 35% in males and 41% in females).[20,21] This, in part, may account for the concerns of clinicians in prescribing diuretics, as hyperuricemia may be a diuretic-related side effect. Stroke is highly correlated with elevated blood pressure, and CCBs have been shown to provide a greater reduction in the risk of stroke (13.5%) than BBs and diuretics.[6] Taiwan has a high prevalence rate (5.95/1000) of stroke, and thus, CCBs seem to be suitable antihypertensive drugs for prevention of stroke.[22]

In Taiwan, we found that cardiologists prescribe more BBs than non-cardiologists. According to the treatment guidelines of the United States and Europe, BBs are recommended as first-line anti-hypertensive drugs.[12,13] However, the latest published European guidelines downgraded their recommendation and withdrew their recommendation of using combination therapy with diuretics and BBs to avoid the negative side effects on lipid profiles and increased incidence of new onset diabetes.[13] Recently, the National Institute for Health and Care Excellence (NICE) guidelines also downgraded their recommendations in regards to the use of BBs in the treatment of hypertension.[23] This decision was based on the findings of a meta-analysis that found them to be the least cost-effective treatment for hypertension, and

notably less effective than the other recommended first-line drugs.[24] Also, BBs were found to be significantly worse at preventing stroke than other drugs.[25] However, most of the evidence for these observations came from trials where atenolol was the BB being used. Thus, these findings may not apply to vasodilating BBs, such as carvedilol and nebivolol.

Compared to the United States, ACE inhibitors were prescribed less than ARBs in Taiwan. This may be related to the widespread intolerance of patients to dry cough, a side effect of ACE inhibitors, which is reported to occur at a rate of 11% in Taiwanese patients.[26]

Limitation

Except for renal function, no other target organ damage was evaluated in detail in this study. However, for those high risk patients that were clarified clearly, it is sufficient to use analysis of BP control rate and prescription patterns in these high risk patients. We did not collect the data of dosage used in each antihypertensive regimen; it may somewhat have influenced the BP control rate of this study.

Summary

In general, Taiwanese physicians follow the current hypertension treatment guidelines relatively well, which may have contributed to the high BP control rate of 63%. Conversely, the low rate of achieving hypertension control in the general population in Taiwan may be related to inadequate public education. Thus, emphasizing the importance of adhering to treatment guideline recommendations is of the utmost importance.[27] Effective implementation of national hypertension guidelines for the primary prevention of cardiovascular disease will require a team-based approach that includes patients, their families, and healthcare professionals.[28] Revising the continuing education policy and medical society programs for physicians and the general population, such as the establishment of Taiwanese hypertension management guidelines, will be necessary to enhance hypertension control in Taiwan.[29]

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